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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page for STN Seminar Schedule - N. America
 NEWS  2  DEC 01   ChemPort single article sales feature unavailable
 NEWS  3  JUN 01   CAS REGISTRY Source of Registration (SR) searching
                   enhanced on STN
 NEWS  4  JUN 26   NUTRACEUT and PHARMAML no longer updated
 NEWS  5  JUN 29   IMSCOPROFILE now reloaded monthly
 NEWS  6  JUN 29   EPFULL adds Simultaneous Left and Right Truncation
                   (SLART) to AB, MCLM, and TI fields
 NEWS  7  JUL 09   PATDPAFULL adds Simultaneous Left and Right
                   Truncation (SLART) to AB, CLM, MCLM, and TI fields
 NEWS  8  JUL 14   USGENE enhances coverage of patent sequence location
                   (PSL) data
 NEWS  9  JUL 27   CA/CAplus enhanced with new citing references
 NEWS 10  JUL 16   GBFULL adds patent backfile data to 1855
 NEWS 11  JUL 21   USGENE adds bibliographic and sequence information
 NEWS 12  JUL 28   EPFULL adds first-page images and applicant-cited
                   references
 NEWS 13  JUL 28   INPADOCDB and INPAFAMDB add Russian legal status data
 NEWS 14  AUG 10   Time limit for inactive STN sessions doubles to 40
                   minutes
 NEWS 15  AUG 17   CAS REGISTRY, the Global Standard for Chemical
                   Research, Approaches 50 Millionth Registration
                   Milestone
 NEWS 16  AUG 18   COMPENDEX indexing changed for the Corporate Source
                   (CS) field
 NEWS 17  AUG 24   ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
 NEWS 18  AUG 24   CA/CAplus enhanced with legal status information for
                   U.S. patents

 NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
              AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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FILE 'HOME' ENTERED AT 07:58:26 ON 09 SEP 2009

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.22       0.22

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FILE 'BIOSIS' ENTERED AT 07:58:42 ON 09 SEP 2009
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=> HCV (l) mutat$3
 95% OF LIMIT FOR TOTAL ANSWERS REACHED
L1    11291029 3

=> adapt$4
SYSTEM LIMITS EXCEEDED - SEARCH ENDED
The search profile you entered was too complex or gave too many
answers.  Simplify or subdivide the query and try again.  If you have
exceeded the answer limit, enter DELETE HISTORY at an arrow prompt
(=>) to remove all previous answers sets and begin at L1.  Use the
SAVE command to store any important profiles or answer sets before
using DELETE HISTORY.

=> L1 and adapt$4
SYSTEM LIMITS EXCEEDED - SEARCH ENDED
The search profile you entered was too complex or gave too many
answers.  Simplify or subdivide the query and try again.  If you have
exceeded the answer limit, enter DELETE HISTORY at an arrow prompt
(=>) to remove all previous answers sets and begin at L1.  Use the
SAVE command to store any important profiles or answer sets before
using DELETE HISTORY.

=> adaptive or adapted
L2      288854 ADAPTIVE OR ADAPTED

=> L1 and L2
L3       58156 L1 AND L2

=> NS3 and L3
L4          54 NS3 AND L3

=> NS5 and L4
L5          10 NS5 AND L4

=> S2204I and L3
L6           3 S2204I AND L3

=> Q1067R and L3
L7           1 Q1067R AND L3

=> D L7 IBIB ABS

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2009 ACS on STN
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Full Text | More Like This

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ACCESSION NUMBER:         2005:523226  CAPLUS
DOCUMENT NUMBER:          143:54458
TITLE:                    Replication competent hepatitis C virus genotype 1a
                          with adaptive mutations and methods of use for drug
                          screening and selection of host cell line
INVENTOR(S):              Lemon, Stanley M.; Yi, Minkyung
PATENT ASSIGNEE(S):       Board of Regents, the University of Texas System, USA
SOURCE:                   PCT Int. Appl., 102 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
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FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053516	A2	20050616	WO 2004-US40120	20041201
WO 2005053516	A3	20051229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1694694	A2	20060830	EP 2004-812596	20041201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 20070292840	A1	20071220	US 2007-580979	20070409
PRIORITY APPLN. INFO.:			US 2003-525989P P	20031201
			WO 2004-US40120 W	20041201

AB The invention provides replication competent polynucleotides that include a coding sequence encoding a hepatitis C virus polyprotein having **adaptive** mutations. The genotype 1a **adaptive** mutations identified here can be grouped functionally into two groups: K2040R, F2080V, and S2204I, which are all located within NS5A, and **Q1067R**, G1188R, V1655I, and K1691R (in NS4A), which are all located in or assocd. with the protease domain of NS3. These NS3 and NS4A mutations are located at some distance from other genotype 1a **adaptive** mutations in NS3 that were previously described. The contribution of the NS5A **adaptive** mutations to the replication of genotype 1a RNA appears to be additive to that of the NS3/4A mutations and not synergistic as shown for the combination of **Q1067R** and K1691R. The invention also includes methods for making replication competent polynucleotides, identifying a compd. that inhibits replication of a replication competent polynucleotide, selecting a replication competent polynucleotide, and detecting a replication competent polynucleotide.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L6 TRIB ABS 1-3

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

Full Text | Cited References

ACCESSION NUMBER: 2005:523226 CAPLUS
DOCUMENT NUMBER: 143:54458
TITLE: Replication competent hepatitis C virus genotype 1a with **adaptive** mutations and methods of use for drug screening and selection of host cell line
INVENTOR(S): Lemon, Stanley M.; Yi, Minkyung
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053516	A2	20050616	WO 2004-US40120	20041201
WO 2005053516	A3	20051229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1694694	A2	20060830	EP 2004-812596	20041201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 20070292840	A1	20071220	US 2007-580979	20070409
PRIORITY APPLN. INFO.:			US 2003-525989P	P 20031201
			WO 2004-US40120	W 20041201

AB The invention provides replication competent polynucleotides that include a coding sequence encoding a hepatitis C virus polyprotein having **adaptive** mutations. The genotype 1a **adaptive** mutations identified here can be grouped functionally into two groups: K2040R, F2080V, and **S2204I**, which are all located within NS5A, and Q1067R, G1188R, V1655I, and K1691R (in NS4A), which are all located in or assocd. with the protease domain of NS3. These NS3 and NS4A mutations are located at some distance from other genotype 1a **adaptive** mutations in NS3 that were previously described. The contribution of the NS5A **adaptive** mutations to the replication of genotype 1a RNA appears to be additive to that of the NS3/4A mutations and not synergistic as shown for the combination of Q1067R and K1691R. The invention also includes methods for making replication competent polynucleotides, identifying a compd. that inhibits replication of a replication competent polynucleotide, selecting a replication competent polynucleotide, and detecting a replication competent polynucleotide.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

Full Text | Cited References

ACCESSION NUMBER: 2003:318798 CAPLUS
DOCUMENT NUMBER: 139:31658
TITLE: Replication studies using genotype 1a subgenomic hepatitis C virus replicons
AUTHOR(S): Gu, Baohua; Gates, Adam T.; Isken, Olaf; Behrens, Sven-Erik; Sarisky, Robert T.
CORPORATE SOURCE: Department of Virology, The Metabolic and Viral Diseases Center of Excellence in Drug Discovery, GlaxoSmithKline Pharmaceuticals, Collegeville, PA, 19426, USA

SOURCE: Journal of Virology (2003), 77(9), 5352-5359
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recently, cell-based replicon systems for hepatitis C virus (HCV), in which the nonstructural proteins stably replicate subgenomic viral RNA in Huh7 cells, were developed. To date, one limitation of using these replicon systems to advance drug discovery is the inability of other genotypic derivs., beyond those of two distinct strains of genotype 1b (HCV-N and Con1), to stably replicate in Huh7 cells. In this report, we evaluated a series of replicon genotype 1a-1b chimeras, as well as a complete genotype 1a replicon clone. A subgenomic replicon construct contg. only type 1a sequences failed to generate stable colonies in Huh7 cells even after repeated attempts. Furthermore, addn. of an NS5A **adaptive** mutation (**S2204I**) which enhances type 1b replicon efficiency was insufficient to confer replication to the wild-type 1a replicon. This subgenomic replicon was subsequently found to be inefficiently translated in Huh7 cells compared to a type 1b replicon, and the attenuation of translation mapped to the N-terminal region of NS3. Therefore, to ensure efficient translation and thereby support replication of the 1a genome, the coding sequence for first 75 residues from type 1a were replaced with the type 1b (strain Con 1) NS3 coding sequence. Although nonstructural proteins were expressed at lower levels with this replicon than with type 1b and although the amt. of viral RNA was also severalfold lower (150 copies of pos.-strand RNA per cell), the replicon stably replicated in Huh7 cells. Notwithstanding this difference, the ratio of pos.- to neg.-strand RNA of 26 was similar to that found with the type 1b replicon. Similar results were found for a 1b replicon expressing the type 1a RNA-dependent RNA polymerase. These 1a hybrid replicons maintained sensitivity to alpha interferon (IFN-α), albeit with an eightfold-higher 50% inhibitory concn. than type 1b replicons. Evidence is provided herein to confirm that this differential response to IFN-α may be attributed directly to the type 1a polymerase.

OS.CITING REF COUNT: 38 THERE ARE 38 CAPLUS RECORDS THAT CITE THIS RECORD (38 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

Full Text | Cited References

ACCESSION NUMBER: 2004:124128 BIOSIS
DOCUMENT NUMBER: PREV200400117042
TITLE: Introduction of NS5A mutations enables subgenomic HCV-replicon1 derived from chimpanzee-infectious HC-J4 isolate to replicate efficiently in HUH-7 cells.
AUTHOR(S): Maekawa, Shinya [Reprint Author]; Enomoto, Nobuyuki [Reprint Author]; Sakamoto, Naoya [Reprint Author]; Kurosaki, Masayuki [Reprint Author]; Ueda, Eri [Reprint Author]; Kohashi, Takahiro [Reprint Author]; Watanabe, Hideki [Reprint Author]; Chen, Cheng-Hsin [Reprint Author]; Yamashiro, Tsuyoshi [Reprint Author]; Tanabe, Yoko [Reprint Author]; Kanazawa, Nobuhiko [Reprint Author]; Nakagawa, Mina [Reprint Author]; Watanabe, Mamoru [Reprint Author]
CORPORATE SOURCE: Tokyo Medical and Dental University, Tokyo, Japan
SOURCE: Hepatology, (October 2003) Vol. 38, No. 4 Suppl. 1, pp. 459A. print.
Meeting Info.: 54th Annual Meeting of the American Association for the Study of Liver Diseases. Boston, MA,

USA. October 24-28, 2003. American Association for the Study of Liver Diseases.
ISSN: 0270-9139 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2004
Last Updated on STN: 3 Mar 2004

AB BACKGROUND: Hepatitis C virus (HCV) subgenomic replicon has been reported to replicate efficiently and continuously in human hepatoma Huh-7 cells. However, several features of this replicon system remain unexplained. First, functional replicons are limited to several HCV clones. In addition, designated cell culture-**adaptive** amino acid mutations in nonstructural (NS) regions are required for efficient replication. To extend the previous results to other isolated HCV clones, we have constructed another HCV replicon from HC-J4, one of the chimpanzee-infectious HCV-1b clones. METHODS: An HCV-replicon derived from HC-J4 (RpJ4) consists of HCV-5'-UTR, neomycin phosphotransferase gene, the encephalomyocarditis virus IRES, HCV-NS3 to NS5B, and HCV-**3**'-UTR. The **adaptive** mutations of NS5A known to be required for HCV-Con1 replicon were introduced in RpJ4 replicon, aa.(amino acids number according to HC-J4) 2197 serine to proline, deletion of serine at aa.2201, and aa.2204 serine to isoleucine (RpJ4-S2197P, RpJ4-S22001del, and RpJ4-**S2204I**). RpJ4/ISDRmutant and RpJ4-S2201del/ISDRmutant were also constructed by introducing six amino acid mutations into the interferon sensitivity determining region (ISDR). In order to know the effect of mutations other than NS5A, a NS5B mutation (aa.2884 arginine to glycine), reported to be highly **adaptive** for HCV-Con1 replicon, was also introduced in RpJ4 (RpJ4-R2884G). Replicon RNA was transfected into Huh-7 cells, and stable replicon-expressing cell lines were established by G418 selection. RESULTS: RpJ4, RpJ4/ISDRmutant, and RpJ4-R2884G did not produce any G418-resistant colonies after transfection. In contrast, G418-resistant cells were transduced efficiently by RpJ4-S2197P, RpJ4-**S2204I**, RpJ4-S2201del and RpJ4-S2201del/ISDRmutants, with the RpJ4-S2201del/ISDRmutant being most efficient. CONCLUSIONS: The HCV replicon derived from HC-J4 can replicate efficiently following the introduction of **adaptive** mutations into the upstream region of ISDR. Moreover, additional introduction of mutations into ISDR further enhances its replication. These findings demonstrate that the genetic structure of the NS5A domain is critical in HCV-1b replications.

=> D L5 IBIB ABS 1-10

L5 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

Full Text | More Like This | References

ACCESSION NUMBER: 2009:526973 CAPLUS
DOCUMENT NUMBER: 150:469293
TITLE: Genomic epidemiology of a dengue virus epidemic in urban Singapore
AUTHOR(S): Schreiber, Mark J.; Holmes, Edward C.; Ong, Swee Hoe; Soh, Harold S. H.; Liu, Wei; Tanner, Lukas; Aw, Pauline P. K.; Tan, Hwee Cheng; Ng, Lee Ching; Leo, Yee Sin; Low, Jenny G. H.; Ong, Adrian; Ooi, Eng Eong; Vasudevan, Subhash G.; Hibberd, Martin L.
CORPORATE SOURCE: Novartis Institute for Tropical Diseases, Singapore, 138670, Singapore
SOURCE: Journal of Virology (2009), 83(9), 4163-4173
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dengue is one of the most important emerging diseases of humans, with no preventative vaccines or antiviral cures available at present. Although one-third of the world's population live at risk of infection, little is known about the pattern and dynamics of dengue virus (DENV) within outbreak situations. By exploiting genomic data from an intensively studied major outbreak, the mol. epidemiol. of DENV could be described at a uniquely fine-scaled temporal and spatial resoln. Two DENV serotypes (DENV-1 and DENV-3), and multiple component genotypes, spread concurrently and with similar epidemiol. and evolutionary profiles during the initial outbreak phase of a major dengue epidemic that took place in Singapore during 2005. Although DENV-1 and DENV-3 differed in viremia and clin. outcome, there was no evidence for **adaptive** evolution before, during, or after the outbreak, indicating that ecol. or immunol. rather than virol. factors were the key determinants of epidemic dynamics.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
Full Text | More Like This | References
ACCESSION NUMBER: 2008:1361945 CAPLUS
DOCUMENT NUMBER: 150:48781
TITLE: Group A human rotavirus genomics: evidence that gene constellations are influenced by viral protein interactions
AUTHOR(S): Heiman, Erica M.; McDonald, Sarah M.; Barro, Mario; Taraporewala, Zenobia F.; Bar-Magen, Tamara; Patton, John T.
CORPORATE SOURCE: Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, 20892-8026, USA
SOURCE: Journal of Virology (2008), 82(22), 11106-11116
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Group A human rotaviruses (HRVs) are the major cause of severe viral gastroenteritis in infants and young children. To gain insight into the level of genetic variation among HRVs, we detd. the genome sequences for 10 strains belonging to different VP7 serotypes (G types). The HRVs chosen for this study, D, DS-1, P, ST3, IAL28, Se584, 69M, WI61, A64, and L26, were isolated from infected persons and **adapted** to cell culture to use as serotype refs. Our sequencing results revealed that most of the individual proteins from each HRV belong to one of three genotypes (1, 2, or 3) based on their similarities to proteins of genogroup strains (Wa, DS-1, or AU-1, resp.). Strains D, P, ST3, IAL28, and WI61 encode genotype 1 (Wa-like) proteins, whereas strains DS-1 and 69M encode genotype 2 (DS-1-like) proteins. Of the 10 HRVs sequenced, 3 of them (Se584, A64, and L26) encode proteins belonging to more than one genotype, indicating that they are intergenogroup reassortants. We used amino acid sequence alignments to identify residues that distinguish proteins belonging to HRV genotype 1, 2, or 3. These genotype-specific changes cluster in definitive regions within each viral protein, many of which are sites of known protein-protein interactions. For the intermediate viral capsid protein (VP6), the changes map onto the at. structure at the VP2-VP6,

VP4-VP6, and VP7-VP6 interfaces. The results of this study provide evidence that group A HRV gene constellations exist and may be influenced by interactions among viral proteins during replication.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

Full Text | Other Sources

ACCESSION NUMBER: 2006:483698 CAPLUS
DOCUMENT NUMBER: 144:482205
TITLE: Hepatitis C virus synthetic variants capable of replication and transfection but having no virulence, and diagnostic, therapeutic and vaccine uses
INVENTOR(S): Rice, Charles M., III; Blight, Keril J.
PATENT ASSIGNEE(S): Washington University, USA
SOURCE: U.S., 84 pp., Cont.-in-part of U.S. Ser. No. 34,756.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7049428	B1	20060523	US 2000-576989	20000523
US 6392028	B1	20020521	US 1998-34756	19980304
CA 2409873	A1	20011129	CA 2001-2409873	20010523
WO 2001089364	A2	20011129	WO 2001-US16822	20010523
WO 2001089364	A3	20030123		
WO 2001089364	A9	20030710		
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EP 1296998	A2	20030402	EP 2001-937697	20010523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003533232	T	20031111	JP 2001-585612	20010523
JP 4095303	B2	20080604		
AU 2001263407	B2	20061207	AU 2001-63407	20010523
AU 2001263407	B9	20070524		
IL 152671	A	20090901	IL 2001-152671	20010523
US 7338759	B1	20080304	US 2003-276051	20030401
US 20060019245	A1	20060126	US 2005-173792	20050701
US 7407758	B2	20080805		
JP 2007143553	A	20070614	JP 2006-339705	20061218
US 20080213750	A1	20080904	US 2007-960391	20071219

PRIORITY APPLN. INFO.:

US 1998-34756	A2	19980304
US 1997-39843P	P	19970304
US 1997-811566	A1	19970304
US 2000-576989	A	20000523

JP 2001-585612	A3	20010523
WO 2001-US16822	W	20010523
US 2003-276051	A1	20030401

AB The invention provides materials and methodologies relating to the prodn. of hepatitis C virus (HCV) variants useful for diagnostic, therapeutic and vaccines. More specifically, the invention provides DNA encoding non-naturally occurring HCV that is capable of replication, have a transfection efficiency and ability to survive subpassage greater than HCV that have wild-type polyprotein coding region. Examples of these **adaptive** mutations are those that encode an amino acid sequence change selected from the group consisting of Ser-1179 to Ile, Arg-1164 to Gly, Ala-1174 to Ser, Ser-1172 to Cys, and Ser-1172 to Pro in NS5A protein. Other **adaptive** mutations may comprise deletion of the ISDR (interferon-sensitivity-detg. region) comprising nucleotides 5345-5485. Expression vectors comprising the above DNA and HCV variants are also described, as are the provision of cells and host cells comprising the expression vectors. Methods for identifying a cell line that is permissive for infection with HCV are also provided, as are vaccines comprising the above polynucleotides in a pharmaceutically acceptable carrier. Addnl., methods for inducing immunoprotection to HCV in a primate are described, as are methods for testing a compd. for inhibiting HCV replication.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 125 THERE ARE 125 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

Full Text | Cited References

ACCESSION NUMBER: 2004:830761 CAPLUS
DOCUMENT NUMBER: 141:422218
TITLE: The molecular epidemiology of dengue virus serotype 4 in Bangkok, Thailand
AUTHOR(S): Klungthong, Chonticha; Zhang, Chunlin; Mammen, Mammen P.; Ubol, Sukathida; Holmes, Edward C.
CORPORATE SOURCE: Department of Virology, U.S. Army Medical Component-Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand
SOURCE: Virology (2004), 329(1), 168-179
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dengue represents a major public health problem in Thailand, with all four viral serotypes co-circulating. Dengue virus serotype 4 (DENV-4) is the least frequently sampled serotype, although one that is often assocd. with hemorrhagic fever during secondary infection. To det. the evolutionary forces shaping the genetic diversity of DENV-4, and particularly whether its changing prevalence could be attributed to instances of **adaptive** evolution in the viral genome, authors undertook a large-scale mol. epidemiol. anal. of DENV-4 in Bangkok, Thailand, using both E gene and complete coding region sequences. This anal. revealed extensive genetic diversity within a single locality at a single time, including the discovery of a new and divergent genotype of DENV-4, as well as a pattern of continual lineage turnover. Authors also recorded the highest av. rate of evolutionary change for this serotype, at 1.072 × 10-3 nucleotide substitutions per site, per yr. However, despite this abundant genetic variation, there was no evidence for **adaptive** evolution in any

gene, codon, or lineage of DENV-4, with the highest rate of nonsynonymous substitution obsd. in NS2A. Consequently, the rapid turnover of DENV-4 lineages through time is most likely the consequence of a high rate of deleterious mutation in the viral genome coupled to seasonal fluctuations in the size of the vector population.

OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:582004 CAPLUS
DOCUMENT NUMBER: 140:92484
TITLE: Screening for T cell-eliciting proteins of Japanese encephalitis virus in a healthy JE-endemic human cohort using recombinant baculovirus-infected insect cell preparations
AUTHOR(S): Kumar, P.; Uchil, P. D.; Sulochana, P.; Nirmala, G.; Chandrashekar, R.; Haridattatreya, M.; Satchidanandam, V.
CORPORATE SOURCE: Department of Microbiology and Cell Biology, Indian Institute of Science, Bangalore, India
SOURCE: Archives of Virology (2003), 148(8), 1569-1591
CODEN: ARVIDF; ISSN: 0304-8608
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The anal. of cell-mediated immune responses in virus-exposed but healthy individuals may contribute to define the features of the T cell response assocd. with resistance. The authors report, for the first time, on **adaptive** T cell responses to 5 largest of the 10 proteins that together constitute 76% of the coding potential of the Japanese encephalitis virus (JEV) genome in a naturally exposed healthy JE-immune human cohort. Fixed and sonified whole cell prepns. of insect cells individually expressing recombinant prM, E, NS1, **NS3** and **NS5** proteins of JEV were used in vitro to stimulate lymphocytes from individuals who had experienced subclin. JEV infections. **NS3**-specific memory T cells were detected in up to 86% of the JEV-infected cohort whereas prM, E and NS1 each elicited reactions in approx. 45% among individuals tested, suggesting that **NS3** is an important target for JEV-specific cell-mediated immune responses. Responses to **NS5**, the largest viral protein were in contrast the poorest, seen in only 13% of the cohort. Moreover, **NS3** stimulated interferon-γ prodn. in both CD4+ and CD8+ T cells indicating that a Th1 immune response to the **NS3** protein may be a crit. determinant of immune control of JEV infection.

OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:521428 CAPLUS
DOCUMENT NUMBER: 138:35963
TITLE: Phylogenetic evidence for **adaptive** evolution of Dengue viruses in nature
AUTHOR(S): Twiddy, S. Susanna; Woelk, Christopher H.; Holmes,

Edward C.
CORPORATE SOURCE: Department of Zoology, University of Oxford, Oxford, OX1 3PS, UK
SOURCE: Journal of General Virology (2002), 83(7), 1679-1689
CODEN: JGVIAY; ISSN: 0022-1317
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A max.-likelihood approach was used to analyze selection pressures acting on genes from all four serotypes of dengue virus (DEN). A no. of amino acid positions were identified within the envelope (E) glycoprotein that have been subject to relatively weak pos. selection in both DEN-3 and DEN-4, as well as in two of the five genotypes of DEN-2. No pos. selection was detected in DEN-1. In accordance with the function of the E protein as the major antigenic determinant of DEN, the majority of these sites were located in, or near to, potential T- or B-cell epitopes. A smaller no. of selected sites was located in other well-defined functional domains of the E protein, suggesting that cell tropism and virus-mediated membrane fusion may also confer fitness advantages to DEN in nature. Several pos. selected amino acid substitutions were also identified in the NS2B and **NS5** genes of DEN-2, although the cause of this selection is unclear, whereas the capsid, membrane and non-structural genes NS1, NS2A, **NS3** and NS4 were all subject to strong functional constraints. Hence, evidence was found for localized **adaptive** evolution in natural isolates of DEN, revealing that selection pressures differ among serotypes, genotypes and viral proteins.
OS.CITING REF COUNT: 30 THERE ARE 30 CAPLUS RECORDS THAT CITE THIS RECORD (30 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Full Text | Cited References

ACCESSION NUMBER: 2006:499431 BIOSIS
DOCUMENT NUMBER: PREV200600505751
TITLE: Differential antigenic hierarchy and T cell threshold associated with spontaneous recovery from HCV infection: Implications for vaccine design.
AUTHOR(S): Smyk-Pearson, Susan; Lezotte, Dennis; Rosen, Hugo
SOURCE: Gastroenterology, (APR 2006) Vol. 130, No. 4, Suppl. 2, pp. A766.
Meeting Info.: Digestive Disease Week Meeting/107th Annual Meeting of the American-Gastroenterological-Association. Los Angeles, CA, USA. May 19 -24, 2006. Amer Gastroenterol Assoc Inst.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Oct 2006
Last Updated on STN: 4 Oct 2006
AB Background: In some exposed individuals, the **adaptive** immune response can spontaneously eradicate HCV infection. Development of vaccine candidates to prevent spread of this disease remains a top priority. Methods: We synthesized 750 genotype la peptides spanning the entire HCV genome (15 mer-peptides, overlapping by 11 amino acids, aa), and these were pooled into 33 distinct subgenomic pools. Using a highly sensitive IFN-gamma ELISPOT assay, we characterized total and sub-genomic HCV-specific CD4+ and CD8+ T cell responses in a cohort of HLA diverse

subjects with chronic (n = 25) and spontaneously resolved (n = 25) infection. Results: Receiver operating characteristic (ROC) analyses were used to display the results of sensitivity and the false positive error rate (1- specificity) of CD4+ and CD8+ T cell responses as predictors of spontaneous recovery. Total HCV-specific CD4+ T cell IFN-producing responses were highly predictive (area under ROC curve = .912, p < .0001) of recovery as were responses to individual gene products, in particular nonstructural (NS) **3** and **NS5**. The cut-off value for total HCV-specific CD4+ T cells where the false positive error rate is minimum and sensitivity is maximum is 752 HCV-specific CD4+ T cells//106 total CD4+ T cells). Individuals exposed to HCV who exceeded this threshold are 23-fold more likely to resolve HCV infection spontaneously as compared to those individuals who did not. Further, we built a mathematical model that was highly predictive of recovery (P < .0001, AUROC 0.89) using CD4+ T cell responses to E1A (aa 193-299), **NS3** 3H (aa 1173-1279), and **NS3** 5H (aa 1369-1479). As shown in Table, there were 8 probability levels with different sensitivity/specificity levels based on the combinations of responses to these three pools. Conclusions: By performing whole HCV genome mapping, this study provides the first clear evidence that a quantitative T cell threshold exists above which spontaneous recovery occurs following HCV infection. Regions identified as highly immunogenic might represent indispensable components of a prophylactic vaccine. Probability and sensitivity parameters of **3**-variable model.

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Full Text | Cited References

ACCESSION NUMBER: 2005:559278 BIOSIS
DOCUMENT NUMBER: PREV200510339116
TITLE: **Adaptive** T cell response in acute hepatitis C.
AUTHOR(S): Kaplan, David E. [Reprint Author]; Sugimoto, Kazushi; Newton, Kimberly; Aytaman, Ayse; Nunes, Frederick; Lucey, Michael; Reddy, K. Rajender; McKeating, Jane A.; Chang, Kyong-Mi
CORPORATE SOURCE: Univ Penn, Philadelphia, PA 19104 USA
SOURCE: Hepatology, (OCT 2005) Vol. 42, No. 4, Suppl. 1, pp. 545A. Meeting Info.: 56th Annual Meeting of the American-Association-for-the-Study-of-Liver-Diseases. San Francisco, CA, USA. November 11 -15, 2005. Amer Assoc Study Liver Dis.
CODEN: HPTLD9. ISSN: 0270-9139.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Dec 2005
Last Updated on STN: 7 Dec 2005

L5 ANSWER 9 OF 10 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

Full Text | Cited References

ACCESSION NUMBER: 2003:502124 BIOSIS
DOCUMENT NUMBER: PREV200300504028
TITLE: Screening for T cell-eliciting proteins of Japanese encephalitis virus in a healthy JE-endemic human cohort using recombinant baculovirus-infected insect cell preparations.
AUTHOR(S): Kumar, P.; Uchil, P. D.; Sulochana, P.; Nirmala, G.; Chandrashekar, R.; Haridattatreya, M.; Satchidanandam, V. [Reprint Author]
CORPORATE SOURCE: Department of Microbiology and Cell Biology, Indian

Institute of Science, Sir C. V. Raman Avenue, Bangalore, KRN, 560012, India
vijaya@mcbl.iisc.ernet.in
SOURCE: Archives of Virology, (August 2003) Vol. 148, No. 8, pp. 1569-1591. print.
CODEN: ARVIDF. ISSN: 0304-8608.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Oct 2003
Last Updated on STN: 29 Oct 2003
AB The analysis of cell-mediated immune responses in virus-exposed but healthy individuals may contribute to define the features of the T cell response associated with resistance. We report, for the first time, on **adaptive** T cell responses to 5 largest of the 10 proteins that together constitute 76% of the coding potential of the Japanese encephalitis virus (JEV) genome in a naturally exposed healthy JE-immune human cohort. Fixed and sonified whole cell preparations of insect cells individually expressing recombinant prM, E, NS1, **NS3** and **NS5** proteins of JEV were used in vitro to stimulate lymphocytes from individuals who had experienced subclinical JEV infections. **NS3**-specific memory T cells were detected in up to 86% of the JEV-infected cohort whereas prM, E and NS1 each elicited reactions in approximately 45% among individuals tested, suggesting that **NS3** is an important target for JEV-specific cell-mediated immune responses. Responses to **NS5**, the largest viral protein were in contrast the poorest, seen in only 13% of the cohort. Moreover, **NS3** stimulated interferon-gamma production in both CD4+ and CD8+ T cells indicating that a Th1 immune response to the **NS3** protein may be a critical determinant of immune control of JEV infection.

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STN

ACCESSION NUMBER: 2002:427645 BIOSIS
DOCUMENT NUMBER: PREV200200427645
TITLE: Phylogenetic evidence for **adaptive** evolution of dengue viruses in nature.
AUTHOR(S): Twiddy, S. Susanna [Reprint author]; Woelk, Christopher H.; Holmes, Edward C.
CORPORATE SOURCE: Department of Zoology, University of Oxford, South Parks Road, Oxford, OX1 3PS, UK
Susanna.Twiddy@zoo.ox.ac.uk
SOURCE: Journal of General Virology, (July, 2002) Vol. 83, No. 7, pp. 1679-1689. print.
CODEN: JGVIAY. ISSN: 0022-1317.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Aug 2002
Last Updated on STN: 7 Aug 2002
AB A maximum-likelihood approach was used to analyse selection pressures acting on genes from all four serotypes of dengue virus (DEN). A number of amino acid positions were identified within the envelope (E) glycoprotein that have been subject to relatively weak positive selection in both DEN-**3** and DEN-4, as well as in two of the five genotypes of DEN-2. No positive selection was detected in DEN-1. In accordance with the function of the E protein as the major antigenic determinant of DEN, the majority of these sites were located in, or near to, potential T- or B-cell epitopes. A smaller number of selected sites was located in other well-defined functional domains of the E protein, suggesting that cell tropism and virus-mediated membrane fusion may also confer fitness

advantages to DEN in nature. Several positively selected amino acid substitutions were also identified in the NS2B and **NS5** genes of DEN-2, although the cause of this selection is unclear, whereas the capsid, membrane and non-structural genes NS1, NS2A, **NS3** and NS4 were all subject to strong functional constraints. Hence, evidence was found for localized **adaptive** evolution in natural isolates of DEN, revealing that selection pressures differ among serotypes, genotypes and viral proteins.

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L8 1 L4 AND Q1067R

=> D L8 IBIB ABS

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2009 ACS on STN

Full Text | More References

ACCESSION NUMBER: 2005:523226 CAPLUS
DOCUMENT NUMBER: 143:54458
TITLE: Replication competent hepatitis C virus genotype 1a with **adaptive** mutations and methods of use for drug screening and selection of host cell line
INVENTOR(S): Lemon, Stanley M.; Yi, Minkyung
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053516	A2	20050616	WO 2004-US40120	20041201
WO 2005053516	A3	20051229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1694694	A2	20060830	EP 2004-812596	20041201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 20070292840	A1	20071220	US 2007-580979	20070409
PRIORITY APPLN. INFO.:			US 2003-525989P	P 20031201
			WO 2004-US40120	W 20041201

AB The invention provides replication competent polynucleotides that include a coding sequence encoding a hepatitis C virus polyprotein having **adaptive** mutations. The genotype 1a **adaptive** mutations identified here can be grouped functionally into two groups: K2040R, F2080V, and S2204I, which are all located within NS5A, and **Q1067R**, G1188R, V1655I, and K1691R (in NS4A), which are all located in or assocd. with the protease domain of **NS3**. These **NS3** and NS4A mutations are located at some distance from other genotype 1a **adaptive** mutations in **NS3** that

were previously described. The contribution of the NS5A **adaptive** mutations to the replication of genotype 1a RNA appears to be additive to that of the **NS3**/4A mutations and not synergistic as shown for the combination of **Q1067R** and K1691R. The invention also includes methods for making replication competent polynucleotides, identifying a compd. that inhibits replication of a replication competent polynucleotide, selecting a replication competent polynucleotide, and detecting a replication competent polynucleotide.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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